

ABSTRACT OF THE DISCLOSURE

The present invention relates to methods and compositions for inhibiting proliferation and inducing cell death in a population of cancer cells by (i) increasing the amount of the differentiation associated protein *MDA-7*, and (ii) decreasing RAS activity within the population. It is based, at least in part, on the discovery that decreasing expression of a mutated, activated *K-ras* gene, together with introducing an expressible *mda-7* gene, in pancreatic cells had a synergistic growth-inhibitory and anti-survival effect, and abolished tumorigenicity of the cells in athymic nude mice. The methods of the invention may be directed to the therapy of pancreatic cancer and other malignancies.